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61241.000016 PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

KOICHIRO MIYAKE, ET AL.

Application No.: 09/673,198

Filed: October 12, 2000

For: A PROCESS FOR PRODUCING ISOPRENOID COMPOUNDS BY MICROORGANISMS AND A METHOD FOR SCREENING COMPOUNDS WITH ANTIBIOTIC OR WEEDING ACTIVITY

Examiner: Tekchand Saidha

Group Art Unit: 1652

Confirmation No. 2149

April 1, 2003

Commissioner for Patents
Washington, D.C. 20231

PETITION UNDER 37 C.F.R. § 1.136(a)
and
RESPONSE TO RESTRICTION REQUIREMENT

Sir:

Applicant petitions the Commissioner for Patents to extend the time for response to the Office Action dated February 14, 2003 (Paper No. 7) for one (1) month, up to and including April 14, 2003. Submitted herewith is a check for $110.00 to cover the fee for the extension under 37 C.F.R. § 1.17. Any deficiency in or overpayment of this fee should be charged or credited to Deposit Account No. 06-1205.

Applicants respond to the Official Action dated February 14, 2003 (Paper No. 7) in the above-identified application, as follows.

REMARKS

In the outstanding Office Action, the Examiner required that Applicants elect for prosecution one of the inventions among Groups I-XXIV for the reasons noted.

As the Examine is aware, the present application is a national stage of a prior PCT application. Accordingly, review of restriction requirement is provided under MPEP §1893.03(d). In support of restriction, regarding Group VIII, the Examiner states

> Group VIII has a special technical feature of a process for making isoprenoid compound using a DNA sequence encoding the protein or enzyme of SEQ ID NO:30 which Groups I-VII and IX-XXIV do not share.

While the Examiner's statement is correct as far as it goes, it is both circular, and respectfully submitted, off point.

As described in the International Preliminary Examination Report[1/] and the International Search Report of the present application, the inventions as set forth in claims 1-9 and 12 (in part) do have a common technical matter of elevating the productivity of isoprenoid compounds through a DNA encoding an enzyme in the non-mevalonate pathway. (Under PCT Rule 13.2, the expression "special technical feature" is defined as meaning those technical feature that defines the contribution which each claimed, considered as a whole, makes over the prior art.)

In particular, Groups V and VIII have a common technical matter of elevating the production of isprenoid compounds using a DNA encoding a protein having activity to catalyze a reaction to produce 2-C-methyl-D-erythritol 4-phosphate from 1-deoxy-D-xyluluse 5-phosphate.

In this regard, both the DNA of SEQ ID NO:31 (Group VIII) and the DNA (*E. coli* yaeM) of SEQ ID NO:10 (Group V) have a feature in common of complementing

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1/ Attached is an English translation of the International Preliminary Examination Report.

methylerythritol-requiring nature of *E. coli* mutant ME7, as seen from Example 1 (2) ② and Example 6 (4) at specification pages 27-29 and 36-37.

Moreover, as described from page 36, line 29 to page 37, line 2, the amino acid sequence encoded by the DNA of SEQ ID NO:31 shares extremely high homology with *E. coli* yaeM protein (SEQ ID NO:5). Therefore, (aside from the fact that MPEP §803.04 makes clear that up to 10 distinct nucleotide sequences are "normally considered"[2/] the same invention, 1192 OG 68 (November 19, 1996)) the DNA of SEQ ID NO:31 and the DNA of SEQ ID NO:10 encode proteins having the same enzymatic activity. Nucleotide sequences encoding the same activity are not generally considered to be independent and distinct. Id.

As described at page 41, lines 24 to 25, *E. coli* yaeM gene product has activity to yield 2-C-methyl-D-erythritol 4-erythritol 4-phosphate from 1-deoxy-D-xylulose 5-phosphahte. Therefore, both the DNA of Group V and the DNA of group VIII belong to the single general inventive concept of "DNA encoding a protein having activity to catalyze a reaction to produce 2-C-methyl-D-erthritol 4-phosphate from 1-deoxy-d-xylulose 5-phosphate".[3/]

Accordingly, at least as to Groups V and VIII, there is a common or corresponding special technical feature and rejoinder thereof is respectfully requested.

Nonetheless, in response to the Office Action, Applicants hereby elect with traverse to prosecute the invention of Group VIII, namely Claims 6-7.

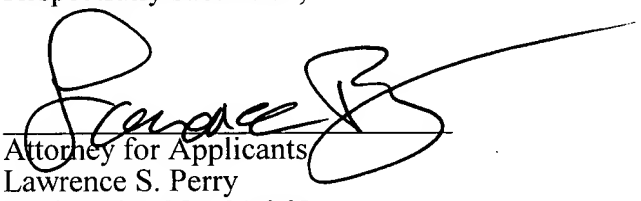
Entry hereof is earnestly solicited.

2/ E.g., when the encoded proteins do not recite disparate three-dimensional folds.

3/ The International Preliminary Examination Report of the present application also indicates that the inventions of claims 6 and 7 have the novelty and the inventive step.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,



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Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rul 70)

Applicant's or agent's file reference PH-635-PCT	FOR FURTHER ACTION	SeeNotificationofTransmittalofInternational Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP99/01987	International filing date (*day/month/year*) 14 April 1999 (14.04.99)	Priority date (*day/month/year*) 14 April 1998 (14.04.98)
International Patent Classification (IPC) or national classification and IPC C12N 15/52, C12P 23/00, C12N 9/00, 9/10, A01N 57/18, C12Q 1/25, 1/48		
Applicant KYOWA HAKKO KOGYO CO., LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06 October 1999 (06.10.99)	12 May 2000 (12.05.2000)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP99/01987

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

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IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☒ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

The requirement of unity of invention in an international application (PCT Rule 13.1) is not satisfied unless a group of inventions as set forth in claims have technical relation to each other involving one or more of the same or corresponding special technical features. The term "special technical feature" means a technical feature that clearly indicates that the inventions as set forth in claims contribute, as a whole, to the prior art (PCT Rule 13.2). The requirement of unity of invention is judged without considering whether a group of inventions is described in separate claims or in one claim in an alternative form (PCT Rule 13.3).

With respect to the claims of the present application, inventions as set forth in claims 1-9 and 12 (in the part where claim 1 is cited) have a technical matter in common of elevating the productivity of isoprenoid compounds by a genetic engineering means with the use of a DNA encoding, for example, an enzyme on the non-mevalonate pathway, while inventions as set forth in claims 14-22 have a technical matter in common that substances inhibiting the enzymatic activity in the non-mevalonate pathway inhibit the growth of microorganisms and plants having this pathway. However, the non-mevalonate pathway has of course been publicly known. Similarly, 1-deoxy-D-xylulose 5-phosphate synthase as an enzyme on the non-mevalonate pathway and the DNA encoding the same have been publicly known [Proc. Natl. Acad. Sci. USA, 94 (24), 12857-12862 (1997)]. Accordingly, it can be concluded that there is no "special technical feature" in common among the inventions as set forth in claims 1-9 and 12 (in the part where claim 1 is cited) and the inventions as set forth in claims 14-22.

In the following description given in claims 10-12 (in the part where claim 11 is cited) and 13:
(i) the invention relating to a protein having an amino acid sequence represented by SEQ ID NO:3 or a DNA having a base sequence represented by SEQ ID NO:8;
(ii) the invention relating to a protein having an amino acid sequence represented by SEQ ID NO:4 or a DNA having a base sequence represented by SEQ ID NO:9; and
(iii) the invention relating to a protein having an amino acid sequence represented by SEQ ID NO:5 or a DNA having a base sequence represented by SEQ ID NO:10;

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☒ all parts.

☐ the parts relating to claims Nos. _____.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box IV (Lack of unity of invention):

have a technical matter in common of being proteins capable of elevating the efficiency of synthesizing isoprenoid compounds or being DNAs encoding the same. Since it is obvious that the above-mentioned publicly-known 1-deoxy-D-xylulose 5-phosphate synthase is one of the proteins having activity capable of elevating the efficiency of biosynthesizing isoprenoid compounds, proteins having activity capable of elevating the efficiency of biosynthesizing isoprenoid compounds or DNAs encoding the same cannot be regarded as any "special technical feature." Moreover, there is no "special technical feature" in common between these groups of inventions (i) to (iii) and the inventions as set forth in claims 1-9 and 12 (in the part where claim 1 is cited) or those as set forth in claims 14-22.

Such being the case, the inventions as set forth in the claims involve five inventions as specified below.

(1) the invention as set forth in claims 1-9 and 12 (in the part where claim 1 is cited);

(2) the invention as set forth in claims 10-12 (in the part where claim 11 is cited) and 13 relating to a protein having an amino acid sequence represented by SEQ ID NO:3 or a DNA having a base sequence represented by SEQ ID NO:8;

(3) the invention as set forth in claims 10-12 (in the part where claim 11 is cited) and 13 relating to a protein having an amino acid sequence represented by SEQ ID NO:4 or a DNA having a base sequence represented by SEQ ID NO:9;

(4) the invention as set forth in claims 10-12 (in the part where claim 11 is cited) and 13 relating to a protein having an amino acid sequence represented by SEQ ID NO:5 or a DNA having a base sequence represented by SEQ ID NO:10: and

(5) the invention as set forth in claims 14-22.

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-12,14-22	YES
	Claims	13	NO
Inventive step (IS)	Claims	6-8,14-22	YES
	Claims	1-5,9-13	NO
Industrial applicability (IA)	Claims	1-22	YES
	Claims		NO

2. Citations and explanations

The subject matters of claims 1-3 and 9 do not appear to involve an inventive step in view of document 1 [Biochemical Journal, Vol. 295, Part 2, 15 October, 1993 (15.10.93), Michel Rohmer et al., "Isoprenoid biosynthesis in bacteria: a novel pathway for the early steps leading to isopentenyl diphosphate," pp. 517-524] and document 2 [Proc. Natl. Acad. Sci. USA, Vol. 94, No. 24, 25 November, 1997 (25.11.97), Georg A. Sprenger et al., "Identification of a thiamin-dependent synthase in Escherichia coli required for the formation of the 1-deoxy-D-xylulose 5-phosphate precursor to isoprenoids, thiamin, and pyridoxol," pp. 12857-12862] respectively cited in the ISR.
Document 1 describes a non-mevalonate pathway in which pyruvic acid and glyceraldehyde 3-phosphate are condensed to produce 1-deoxy-D-xylulose 5-phosphate, for biosynthesizing isopentenyl pyrophosphate (IPP) through it. Document 2 describes a gene encoding 1-deoxy-D-xylulose 5-phosphate synthase. It could have been easily predicted by a person skilled in the art, that if the amount of 1-deoxy-D-xylulose 5-phosphate produced as an intermediate product is increased in the non-mevalonate pathway described in document 1, the produced amount of IPP as a basic structural component of an isoprenoid compound increases, and therefore that the produced amount of an isoprenoid compound increases. So, it is obvious for a person skilled in the art to use the gene described in document 2, for obtaining a transformant increased in the production of an isoprenoid compound by a well-known genetic engineering method, and then to culture it.

The subject matters of claims 1, 4, 5 and 9 do not appear to involve an inventive step in view of document 3 (Journal of Biochemistry, Vol. 108, No. 6, December 1990, Shingo Fujisaki et al., "Cloning and Nucleotide Sequence of the ispA Gene Responsible for Farnesyl Diphosphate Synthase Activity in Escherichia coli," pp. 995-1000) and document 4 [Koso Handbook," supervised by Fumiharu Maruo et al., first edition, 1 December, 1982 (01.12.82), K.K. Asakura Shoten, p. 303] respectively cited in the ISR.
Document 3 describes a DNA encoding a protein [farnesyl pyrophosphate (FPP) synthase] having an amino acid sequence represented by SEQ ID NO:2 of the present application (ORF-2 of Fig. 3), and it is publicly known that FPP synthase is an enzyme for catalyzing the reaction from IPP to FPP, as also described in document 4. It is also publicly known that FPP is an intermediate product in the biosynthesis of various isoprenoids (for example, see "Seikagaku Jiten (2nd edition)" supervised by Kazutomo Imahori et al., 22 November, 1990 (22.11.90), K.K. Tokyo Kagaku Dojin, p. 890). So, it could have been easily predicted by a person skilled in the art that if the production of FPP is increased, the production of an isoprenoid compound would be increased accordingly. So, it is considered to be obvious for a person skilled in the art to use the DNA described in document 3, for obtaining a transformant increased in the production of an isoprenoid compound by a well-known genetic engineering method, and then to culture it.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V (Citations and explanations):

The subject matter of claim 13 does not appear to be novel in view of document 3.
The ORF-1 of Fig. 3 of document 3 is the DNA encoding a protein having an amino acid sequence represented by SEQ ID NO:3 of the present application.

The subject matters of claims 10-12 do not appear to involve an inventive step in view of document 3.
Fig. 3 of document 3 describes an amino acid sequence encoded by the DNA sequence of ORF-1. So, a protein having an amino acid sequence represented by SEQ ID NO:3 and a production process thereof are obvious to a person skilled in the art.

The subject matters of claims 6-8 and 14-22 are neither described in any of the documents cited in the ISR nor obvious to a person skilled in the art from the prior art including these documents.